Letter to the Editor

(discussing Volkow ND, Swanson JM, Evins E, et al. Effects of cannabis use on human behavior, including cognition, motivation, and psychosis: A review. *JAMA Psychiatry*. 2016;73(3):292-297.)

Title: **The effects of cannabis use on human behavior: a call for standardization of cannabis use metrics**

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To the Editor With rapidly shifting legislation worldwide in relation to recreational and medicinal cannabis use, the review by Volkow et al[1] is timely. We highlight several additional noteworthy issues for consideration.

While further evidence has emerged that acute and chronic exposure to cannabis impairs cognition,[2] there is still grossly insufficient evidence for recovery of function with abstinence. Neither the parameters of cannabis exposure nor the neural mechanisms subserving persistence or recovery have been elucidated. Well-controlled prospective studies monitoring restoration of brain function and structure from current use through prolonged abstinence are required to delineate the time course and moderators of potential recovery of cognitive function.

Volkow et al[1] cite evidence that cannabidiol may protect against some harmful cognitive effects. We have evidence that cannabidiol may also protect against structural brain harms[3,4] (eg, hippocampal neural integrity and volume loss in cannabis users[4]) which are also restored with prolonged abstinence.[4] This potential neuroprotective property of cannabidiol is promising for implementation in harm minimization and therapeutic strategies for a range of conditions, including cannabis dependence.

Vokow et al[1] query the generalization of chronic effects on cognition and motivation claiming that many study samples include a large proportion of cannabis dependent individuals. We find that formal diagnostic assessment of

cannabis use disorders is rarely performed in neurocognitive studies[5] and cognitive deficits in recreational users are associated with varying cannabis use parameters.[2] We suggest further investigation of specific neural alterations that dissociate dependence from non-problem use, toward the development of neurobiological models of cannabis addiction and related harms.[3,5]

Acute intoxication broadly impairs multiple aspects of cognition that are likely to affect users in daily life. An assumption that frequent cannabis users develop tolerance to its adverse cognitive effects has little empirical evidence.[2] While cognitive impairments may be blunted in regular users following acute intoxication, they are nevertheless evident across multiple domains (psychomotor, attention, memory), with potential real-world effects on complex tasks such as driving.

We agree with Volkow et al[1] that “there is a need to clarify which aspects of cannabis exposure (eg, age at initiation, quantity used, frequency of use, duration of use, and potency of cannabis used) confer the greatest risk for… adverse consequences”. Further, we advocate for greater standardization of cannabis use metrics by consensus to quantify various parameters of cannabis exposure in humans,[2,3,5] which will serve as a starting point for addressing the many outstanding questions regarding its effects on human behavior.

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